REMARKS

1. Restriction/Election

The Examiner has indicated that Applicant's reading of the Office Action mailed on September 30, 2002 was correct and has agreed to withdraw the species election and combine claims 3-5 together. Thus, claims 1-10 and 14-20 are currently under examination. However, since (as the Examiner agrees) there has been no restriction requirement, only an election of species, once the elected species is found allowable, examination on the merits should proceed to the other species and the generic claims, including claims 11-13 (see MPEP (809-02(c)).

2. Specification

The Examiner has objected to the disclosure because it fails to describe P1 to P14 referenced in Figure 1 and because the Specification does not adequately describe the computer program MASP and where the public can obtain the computer program. Applicant has amended the Specification to address these issues. Reconsideration and removal of the objection is respectfully requested.

3. Drawings

The draftsperson has objected to the drawings as being of poor quality. Applicant hereby submits another set of drawings. Reconsideration and removal of the objection to the drawings is requested.

4. Claim Objections

The Examiner has objected to the claims for a number of informalities. Claims 9 and 15-18 have been objected to as being improper multiple dependent claims. Claim 1 has been objected to because "method" in the preamble should be preceded by "A". Claims 2-8 have been objected to because "method" in the preamble should be preceded by "The". Claims 1, 19 and 20 have been objected to because the phrase "a nucleic acid molecule" in the preamble should be "nucleic acid molecules" and the word "were" in step (b) should be "are". The Examiner also indicates that the phrase "specifically hybridized probe" in step (c) in unclear and should be changed to "the probes that are hybridized" to correspond to the language in step (b) of the

claim. The Examiner further recommends changing the phrase "determination of the nucleic acid molecules by means of the probes hybridized to them" in step (e) to "detection of the nucleotide sequence in the nucleic acid molecules by means of the probes hybridized to the nucleotide sequence" in order to correspond to the recited goal in claims 1, 19 and 20.. Claims 3 and 20 have been objected to for a typographical error and improper antecedent basis support for a number of claim terms. Claim 4 has been objected to because for purposes of clarity and the Examiner suggests inserting the word "by" before "a biotin-streptavidin bond". The Examiner similarly suggests inserting the word "by" before "a Gene-32 nucleic acid bond" to make a better sentence. The Examiner suggests deleting "at the same time" from claim 7 and the word "moreover" from claim 8 to make a better sentence. Claim 19 was objected to because the phrase "are generates" in step (a) should be "are generated". Applicant has amended the claims in the manner suggested by the Examiner. Applicant believes that the foregoing claim amendments have obviated the claim objections raised by the Examiner. Accordingly, reconsideration and removal of the claim objections is respectfully requested.

5. Rejections under 35 U.S.C. §112, second paragraph

Claims 1-8, 19 and 20 have been rejected as indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner has rejected claims 1, 19 and 20 because it is unclear what the relationship between the "hydridized probes" in step (d) and those from step (c). Applicant has amended the claims so that it is now clear that the probes in step (d) are those that have been detached or released from step (c). Claims 2 and 20 were rejected because there is insufficient antecedent basis support for the limitation "the surface of a support" in the claim. Applicant has amended the claims as suggested by the Examiner to overcome the rejection. Applicant believes that the foregoing amendments have overcome all of the indefiniteness rejections. Reconsideration and removal of the rejections is respectfully requested.

Favorable consideration and early allowance of the claims is requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,330) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. § 1.17 and 1.136(a), Applicant hereby petition for an extension of one (1) month to October 3, 2003 for the period in which to file a response to the Office Action dated June 3, 2003.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on: Oct 3 2003
(Date of Deposit)

BIRCH, STEWART, KOLASCH & BIRCH, LLP

Susan Langworthy
(Signature)

Oct 3 2003
(Date of Signature)

AMENDMENTS TO THE SPECIFICATION

On page 13 of the Specification, please replace the description of Figure 1 with the following:

--Figure 1

Scheme of fingerprinting with mass spectrometrical scanning. P1 to P14 refer to different probes contained within the library.

1. Combinatorially generated library of probes that can be differentiated by their mass.
2. The library is hybridized to an immobilized target DNA. After washing it intensively (to remove non-specifically bound probes), the correctly hydridized probes are separated from the target DNA.
3. This solution is [analysed] analyzed in an electrospray mass spectrometer. The partial sequences of the target DNA are determined by clearly allocating the mass to the sequences.—

On page 14 of the Specification, please replace the description of Figure 4 with the following:

--Figure 4

Calculated mass spectrum of a PNA library.
Two different solid phase syntheses (one of which is mass-labelled) with 32 different sequences each make up 64 different mass peaks, each of them being allocated to a specific sequence from a PNA library with 3 variable positions with four bases (A, C, G and T being inserted). The calculation is based on the substituents listed in Table 1. [For the calculations the computer programme MASP (© Dr. Christoph Steinbeck) was used.] The calculations were performed using the computer program MASP, a program which predicts the mass spectra of combinatorial libraries developed by Dr. Christoph Steinbeck (*see C. Steinbeck, K. Berlin, C. Richert, "MASP – A Program Predicting Mass Spectra of Combinatorial Libraries", J. Chem. Inf. Comput. Sci. 1997, 37, 449-457*). The MASP program is free software which may be downloaded from the URL http://134.34.110.44/htdocs/MASP/masp.html.--

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A ~~M~~method for detecting a nucleotide sequence in ~~a~~ nucleic acid molecules comprising the following steps:
   (a) hybridization of nucleic acid molecules to a set of probes of different nucleobase sequences, wherein each probe has a mass that differs from the one of all the other probes;
   (b) separation of the probes that ~~were~~are not hybridized;
   (c) detachment of the probles that are hydridized ~~a specifically hybridized probe~~ in a solvent;
   (d) analysis of the ~~hybridized~~ probes that are detached from step (c) ~~in a solution~~ by means of electrospray mass spectrometry; and
   (e) detecting the nucleotide sequence in the nucleic acid molecules ~~determination of the nucleic acid molecules~~ by means of the probes hybridized to ~~them~~the nucleotide sequence.

2. (Currently Amended) The ~~M~~method according to claim 1, wherein the nucleic acid molecules are immobilized at ~~the~~ a surface of a support before or after step (a).

3. (Currently Amended) The ~~M~~method according to claim 2, wherein the immobilization of the nucleic acid molecules at the surface is carried out via a~~n~~ NH_2, epoxy or SH function by means of coating the surface of the ~~probe~~ supports with a silicate or silane, via a protein-substrate interaction, a protein-protein interaction, ~~or~~ a protein-nucleic acid interaction or via an interaction of two hydrophobic buiilding blocks.

4. (Currently Amended) The ~~M~~method according to claim 3, wherein the protein-substrate interaction is by means of a biotin-streptavidin bond or an antibody-antigen bond.

5. (Currently Amended) The ~~M~~method according to claim 3, wherein the protein-nucleic acid interaction is by means of a Gene32-nucleic acid bond.

6. (Currently Amended) The ~~M~~method according to any one of claims 1 to 5, wherein the probes are nucleic acids having a mass tag.

7. (Currently Amended) The ~~M~~method according to claim 6, wherein the mass tag is ~~at the same time~~also a charge tag.

8. (Currently Amended) The ~~M~~method according to claim 6, wherein the nucleic acids ~~moreover~~ have a charge tag.

9. (Currently Amended) The ~~M~~method according to ~~any one of claims 1 to 8~~ claim 1, wherein the probes are modified nucleic acid molecules.

10. (Currently Amended) The ~~M~~method according to claim 9, wherein the modified nucleic acid molecules are PNAs, alkylated phosphorothioate nucleic acids or alkylphosphonate nucleic acids.

11. (Withdrawn) The ~~M~~method according to ~~any one of claims 1 to 10~~claim 1, wherein the probes are generated by means of combinatorial solid phase synthesis.

12. (Withdrawn) The ~~M~~method according to claim 11, wherein different base builiding blocks are labelled ~~in such a way that~~whereby the probes synthesized therefrom can be differentiated in the mass spectrometer due to their mass.

13. (Withdrawn) The ~~M~~method according to claim 12, wherein the label~~ling~~ is a methyl, ethyl, propyl, a branched or non-branched alkyl, a halogen substituted branched or non-branched alkyl, alkoxyalkyl, alkylaryl, arylalkyl, alkoxyaryl or aryloxyalkyl group or one of their deuterated or other isotopic variants.

14. (Currently Amended) The ~~M~~method according to any one of claims ~~10 to 13~~ 9, wherein the probes have at least one modification in a defined position away from randomized nucleotides allowing for the cleavage of the probe.

15. (Currently Amended) The ~~M~~method according to claim 14, wherein the probes are modified by~~modification means the introduction~~ introducing ~~of~~ a phosphorothioate group, a ~~and/or an~~ RNA base, a ~~and/or a~~ phosphotriester bond or a combination thereof into the probe.

16. (Currently Amended) The ~~M~~method according to ~~any one of claims 1 to 15~~claim 1, wherein the probes are generated as partial libraries having different mass and/or charge tags.

17. (Currently Amended) The ~~M~~method according to ~~any one of claims 1 to 16~~claim 2, wherein the positions of the probes on the ~~probe~~ support allow for an allocation to the nucleic acid molecules hybridizing thereto.

18. (Currently Amended) A ~~K~~kit comprising

(a) a set of probes as defined in ~~any one of~~ claims 6 ~~to 16~~ and/or

(b) a probe support which has been pretreated and thus allows for the attachment of target DNAs and/or target DNAs that have already been attached.

19. (Currently Amended) A method for detecting a nucleotide sequence in ~~a~~ nucleic acid molecules comprising the following steps:

(a) hybridization of nucleic acid molecules to a test set of probes of different nucleobase sequences, wherein each probe has a mass that differs from the one of all the other probes, and wherein the probes are ~~generates~~ generated as partial libraries having different mass and/or charge tags;

(b) separation of the probes that ~~were~~ are not hybridized;

(c) detachment of ~~a specifically hybridized probe~~the probes that are hybridized in a solvent;

(d) analysis of the ~~hybridized~~ probes that are detached from step (c) ~~in a solution~~ by means of electrospray mass spectrometry; and

(e) ~~determination~~ detecting the nucleotide sequence in~~of~~ the nucleic acid molecules by means of the probes hybridized to ~~them~~the nucleotide sequence.

20. (Currently Amended) A method for detecting a nucleotide sequence in ~~a~~ nucleic acid molecules comprising the following steps:

(a) hybridization of nucleic acid molecules to a test set of probes of different nucleobase sequences, wherein each probe has a mass that differs from the one of all the other probes;

(b) immobilization of the nucleic acid molecules of at ~~the~~ a surface of a support before or after step (a) using a~~n~~ NH_2 , epoxy or SH function by means of coating the surface of the ~~probe~~ supports with a silicate or silane, via a protein-substrate interaction, a protein-protein interaction or an interaction of two hydrophobic building blocks;

(c) separation of the probes that ~~were~~are not hybridized;

(d) detachment of the probes that are hybridized ~~a specifically hybridized probe~~ in a solvent;

(e) analysis of the ~~hybridized~~ probes that are detached from step (c) ~~in a solution~~ by means of electrospray mass spectrometry; and

(f) ~~d~~detecting the nucleotide sequence of~~etermination of~~ the nucleic acid molecules by means of the probes hybridized to ~~them~~the nucleotide sequence.